

Listing of Claims:

This listing of claims will replace all prior versions and listings of claims in the application:

1.-20. (Canceled)

21. (Currently Amended) An autoclaved composition of an aqueous injectable, terminally steam sterilized suspension in a vial sealed under nitrogen atmosphere, said suspension consisting essentially of

particles of a water insoluble or poorly soluble biologically active substance with a volume weighted mean particle size of up to 3 μm , with not more than 3000 particles of a size of 10 μm or greater and not more than 300 particles of a size of 25 μm or greater,

said particles surface stabilized with one or more phospholipid surface modifiers, and a pharmaceutically acceptable amount of a water soluble polyhydroxy thermoprotecting agent selected from the group consisting of trehalose, lactose, dextrose, sorbitol, dextran, mannitol and mixtures thereof, wherein said thermoprotecting agent is present in an amount effective to restrict an increase in volume weighted mean diameter of said suspension during and after terminal steam sterilization.

wherein the ratio of said active substance to said phospholipid surface modifier is from about 3:1 to about 5:1 and the amount of said phospholipid surface modifier is in the range from about 0.2% w/w to about 5.0% w/w,

wherein said composition is devoid of surfactants that require during terminal steam sterilization elevation of their cloud point temperature by addition of a cloud point modifier,

said composition being devoid of surfactant additives which coagulate on steam sterilization, and further wherein the volume weighted mean particle size of said particles is not increased more than two-fold during and after terminal steam sterilization, and

wherein the size of said particle is smaller following autoclaving as compared to the size of a particle following autoclaving that consists essentially of said biologically active substance and said phospholipid surface modifier without said thermoprotecting agent.

22. (Currently Amended) An autoclaved composition of an injectable, non-flocculating, aqueous, terminally steam sterilized suspension under nitrogen in a sealed vial, said suspension consisting essentially of

particles of a water insoluble or poorly soluble drug substance with a volume weighted mean particle size of up to 3 μm ,

said particles surface stabilized with one or more phospholipid surface modifiers, and a pharmaceutically acceptable amount of a water soluble polyhydroxy thermoprotecting agent, wherein said thermoprotecting agent is present in an amount effective to restrict an increase in volume weighted mean diameter of said suspension during and after terminal steam sterilization,

wherein (i) the ratio of said drug substance to said surface modifier is about 3:1 to about 5:1,

(ii) the amount of said surface modifier is in the range from about 0.2% w/w to about 5.0% w/w, and

(iii) said volume weighted mean particle size is not increased more than two-fold during and after terminal steam sterilization, and wherein said composition is devoid of surfactants that require during terminal steam sterilization elevation of their cloud point temperature by addition of a cloud point modifier and is devoid of surfactant additives which coagulate on steam sterilization, and the ratio of the amount of the active substance and the thermoprotecting agent is selected to provide particle size stability during and after terminal steam sterilization, and

wherein the size of said particle is smaller following autoclaving as compared to the size of a particle following autoclaving that consists essentially of said drug substance and said phospholipid surface modifier without said thermoprotecting agent.

23. (Previously Presented) The composition according to claim 21 or claim 22, wherein the suspension also includes a nonsurfactant additive to adjust osmotic pressure.
24. (Previously Presented) The composition according to claim 21 or claim 22, wherein the suspension is diluted with water for parenteral administration.
25. -27. (Cancelled).
28. (Previously Presented) The composition according to claim 22, wherein the suspension further comprises a pharmaceutical excipient for ophthalmic, peroral, or transdermal administration of the water insoluble or poorly soluble drug substance.
29. (Previously Presented) The composition according to claim 21, wherein the active substance is an antifungal agent.
30. (Previously Presented) The composition according to claim 29, wherein the antifungal agent is itraconazole.
31. (Previously Presented) The composition according to claim 21, wherein the active substance is an immunosuppressive agent.
32. (Previously Presented) The composition according to claim 21, wherein the active substance is a sterol.
33. (Previously Presented) The composition according to claim 32, wherein the sterol is alfaxalone.
34. (Previously Presented) A lyophilized or spray dried powder prepared from the composition according to claim 22.
35. (Previously Presented) The composition according to claim 22, wherein the water-insoluble or poorly water soluble drug substance is suitable for either immediate release or sustained release delivery of said drug substance by parenteral administration.

36. (Previously Presented) The composition according to claim 35, wherein the parenteral administration is intramuscular, intravenous, or subcutaneous administration.

37. (Previously Presented) The composition according to claim 31, wherein the immunosuppressive agent is a cyclosporin.

38. (Currently Amended) An autoclaved aqueous suspension consisting essentially of (i) particles of a water insoluble or poorly soluble biologically active substance, (ii) from about 0.2 % w/w to about 5 % w/w of one or more phospholipid surface modifiers, and (iii) a pharmaceutically acceptable, water soluble polyhydroxy thermoprotecting agent sealed in a vial under nitrogen atmosphere wherein said thermoprotecting agent is present in an amount effective to restrict an increase in volume weighted mean diameter of said suspension during and after terminal steam sterilization, said suspension containing particles of the water insoluble or poorly soluble biologically active substance, said particles comprising a volume weighted mean particle size of up to 3 μm , with not more than 3000 particles of a size of 10 μm or greater and not more than 300 particles of a size of 25 μm or greater, wherein the ratio of the amount of the active substance to the phospholipid surface modifier and/or the thermoprotecting agent is selected so as to provide particle size stability during and after terminal steam sterilization, and wherein the volume weighted mean particle size subsequent to terminal steam sterilization is not more than about two-fold of the volume weighted mean particle size prior to the terminal steam sterilization, and the suspension is devoid of surfactants which coagulate on steam sterilization, and

wherein the size of said particle is smaller following autoclaving as compared to the size of a particle following autoclaving that consists essentially of said biologically active substance and said phospholipid surface modifier without said thermoprotecting agent.

39. (Cancelled).

40. (Previously Presented) The suspension according to claim 38, wherein the pH of the suspension before terminal steam sterilization is from about 5 to about 9.

41. (Previously Presented) The suspension according to claim 38, further comprising a non-surfactant additive to adjust osmotic pressure of the suspension.
42. (Previously Presented) The suspension according to claim 38, further comprising an amount of a non-surfactant additive such that, on diluting the suspension with a pharmaceutically acceptable diluent suitable for parenteral administration to a pharmaceutically acceptable concentration for parenteral administration, a suitable osmotic pressure of the diluted suspension results.
43. -45. (Cancelled).
46. (Previously Presented) The suspension according to claim 38, wherein the amount of the surface modifier provides a biologically active substance to surface modifier ratio of 3:1 to 5:1.
47. (Cancelled).
48. (Previously Presented) The suspension according to claim 38, further comprising a pharmaceutical excipient for ophthalmic, peroral, or transdermal administration of the water insoluble or poorly soluble biologically active substance.
49. (Previously Presented) The suspension according to claim 38, wherein the active substance is an antifungal agent.
50. (Previously Presented) The suspension according to claim 49, wherein the antifungal agent is itraconazole.
51. (Previously Presented) The suspension according to claim 38, wherein the active substance is an immunosuppressive drug.
52. (Previously Presented) The suspension according to claim 51, wherein the immunosuppressive drug is a cyclosporin.
53. (Previously Presented) The suspension according to claim 38, wherein the active substance is a sterol.

54. (Previously Presented) The suspension according to claim 53, wherein the sterol is alfaxalone.
55. (Cancelled).
56. (Previously Presented) The suspension according to claim 38, wherein the water-insoluble or poorly water-soluble biologically active substance is at a pharmaceutically acceptable concentration for either immediate release or sustained release delivery of the active substance by parenteral administration.
57. (Previously Presented) The suspension according to claim 56, wherein the parenteral administration is intramuscular, intravenous, or subcutaneous administration.
- 58.-62. (Cancelled).
63. (Previously Presented) The aqueous suspension according to claim 38, further wherein the suspension is substantially devoid of surfactants that require elevation of their cloud point temperature by addition of a cloud point modifier for further stabilization.
64. (Previously Presented) The composition according to claim 21, wherein said composition consists of
- said particles of said water insoluble or poorly soluble biologically active substance,
 - said one or more phospholipid surface modifiers, and
 - said polyhydroxy thermoprotecting agent.
65. (Previously Presented) The composition according to claim 22, wherein said composition consists of
- said drug substance,
 - said one or more phospholipid surface modifiers, and
 - saod polyhydroxy thermoprotecting agent.

66. (Previously Presented) The suspension according to claim 38, wherein said composition consists of

- said water insoluble or poorly soluble biologically active substance,
- said one or more phospholipid surface modifiers, and
- said polyhydroxy thermoprotecting agent.

67. (New) The composition of claim 21, wherein the polydroxy thermoprotecting agent is selected from the group consisting of trehalose, lactose, dextrose, sorbitol, dextran, and mixtures thereof.

68. (New) The composition of claim 21, wherein the phospholipid surface modifier is egg phospholipid, soy phospholipid, or Lipoid E80®.

69. (New) The composition of claim 22, wherein the polydroxy thermoprotecting agent is selected from the group consisting of trehalose, lactose, dextrose, sorbitol, dextran, and mixtures thereof.

70. (New) The composition of claim 22, wherein the phospholipid surface modifier is egg phospholipid, soy phospholipid, or Lipoid E80®.

71. (New) The composition of claim 28, wherein the polydroxy thermoprotecting agent is selected from the group consisting of trehalose, lactose, dextrose, sorbitol, dextran, and mixtures thereof.

72. (New) The composition of claim 28, wherein the phospholipid surface modifier is egg phospholipid, soy phospholipid, or Lipoid E80®.

73. (New) The aqueous suspension of claim 22, wherein the suspension lacks glycerol.

74. (New) The aqueous suspension of claim 23, wherein the suspension lacks glycerol.

75. (New) The aqueous suspension of claim 24, wherein the suspension lacks glycerol.